Remarks

Reconsideration of this Application is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 27, 31, 36, 39, 120, 124, 128 and 130 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Savage, WO 99/64464 (hereinafter "Savage"); in view of Cormier *et al.*, *Int. J. Cancer 75*:517-524 (1998) (hereinafter "Cormier"); Schnell *et al.*, *J. Immunol. 164*:1243-1250 (2000) (hereinafter "Schnell"); and Zarour *et al.*, *PNAS 97*:400-405 (2000) (hereinafter "Zarour"). Applicants respectfully traverse this rejection.

The invention is directed to a compound comprising at least one class II MHC complex linked to at least one antibody or fragment thereof, wherein the linkage is through the carboxy terminus of the antibody or fragment thereof. In the presently examined invention, the antibody is specific for the specific tumor marker carcinoembryonic antigen, and the class II MHC complex comprises the specific melanoma antigen MelanA/MART-1 (51-73).

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103, the prior art must teach or suggest all the limitations of the claims. There must also be some suggestion or motivation to combine the teachings or modify the prior art to arrive at the claimed invention. Finally, the teaching or suggestion to modify the prior art must come

from the prior art itself, and not the application *See In re Vaeck*, 20 U.S.P.Q.2d (BNA) 1438 (Fed. Cir. 1991).

Savage is directed to class I MHC complexes linked to an antibody, *not* class II MHC complexes as claimed in the present invention. Nothing in Savage teaches nor suggests changing the complexes described therein to substitute class II MHC complexes for class I MHC complexes. Further, nothing in Savage teaches nor suggests linking a MHC complex with a melanoma antigen to an antibody or fragment thereof which is specific for a surface marker of colon cancer.

Class I and II MHC complexes differ in their structure, and in their function. Class I MHC molecules are composed of a α variable chain, coded for by MHC genes, associated with a non-variable β2-microglobulin, coded for by non-MHC genes. Class I molecules bind peptides of about 8-9 amino acids in length. Class I MHC molecules interact with CD8+ T cells, also known as cytotoxic T cells. Cytotoxic T cells function by lysing target cells in an antigen-dependent manner and are active in cell-mediated immunity. Class I MHC complexes are found on the surface of all cells.

In contrast, class II MHC molecules are composed of two variable chains, the heavy (α) and light (β), both encoded by MHC genes. Class II molecules bind peptides of about 13-18 amino acids in length. Class II MHC molecules interact with CD4+ T cells, also known as T helper cells. T helper cells function by producing cytokines and are active in humoral immunity. Class II MHC complexes are only found on the surface of professional antigen presenting cells.

Cormier is directed to the identification of the prevalance of two melanoma-associated antigen, MelanA/MART-1 and Pmel17/gp100, along with class I MHC

molecules, in samples from patients with metastatic melanoma. Cormier postulates that the downregulation of melanoma antigens, combined with the downregulation of class I MHC molecules, may contribute to tumor escape. Cormier does not mention class II MHC molecules, nor describe their involvement in tumor immunity. Nothing in Cormier teaches nor suggests modifying the compounds of Savage to include class II MHC molecules to arrive at the presently claimed invention.

Schnell is directed to the induction of an immune response by transducing dendritic cells with class I and II MHC-restricted peptides. Dendritic cells are professional antigen presenting cells. According to Schnell, "[t]hese findings have practical implications for the use of DCs to immunize against tumor cells." Schnell at page 1249. Nothing in Schnell teaches or suggests making MHC-peptide complexes, much less MHC-peptide complexes linked to an antibody, because only the antigenic peptides are used. Further, the antigenic peptides are transduced into dendritic cells, not tumor cells, which are the target of the presently claimed invention. Thus, Schnell does not suggest modifying the disclosure of Savage to make the compound of the claims.

Zarour is directed to the identification of a class II MHC epitope encoded by the MART-1 gene. As stated in Zarour, this identification could lead to better clinical strategies "accomplished by vaccination with protein or multivalent peptides including class I- and class II-restricted epitopes . . . in patients with melanoma." Zarour at page 405. Nothing in Zarour teaches or suggests using anything other than peptides or proteins themselves as cancer vaccines. Further, Zarour certainly does not suggest using melanoma antigens in conjunction with antibodies specific for colon cancer. Thus,

Zarour does not suggest modifying the compounds of Savage to arrive at the presently claimed invention.

While Savage teaches certain class I MHC - antibody compounds, nothing in Savage suggests class II MHC - antibody compounds. Nothing in the art suggests modifying Savage to arrive at the presently claimed invention. Specifically, nothing in the art relied upon in the rejection suggests making a compound comprising a class II MHC complex coupled with an antibody, much less a class II MHC - Melan-A/MART-1 (51-73) peptide coupled with an antibody specific for colon cancer.

Applicants submit that the invention is non-obvious over the prior art. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

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